Remarks

Reconsideration and withdrawal of the rejections set forth in the Office action dated August 1, 2006 are respectfully requested. Applicants petition the Commissioner for a 1-month extension of time. A separate petition accompanies this amendment.

Claims 1-38 are pending. Claims 5, 8-10, 12, 14-15, 22-24, 27-28, 32-34, and 36-38 are withdrawn. Claims 39-81 are canceled. Claims 1-4, 6-7, 11, 13, 16-21, 25-26, 29-31, and 35 are under examination.

I. Amendments

Claim 7 is amended for clarity.

Claim 15 is withdrawn.

Withdrawn claim 23 is amended to correct an obvious typographical error.

No new matter is added by way of these amendments.

II. Election/Restriction

Regarding claim 7, Applicants have amended the claim to clarify that the product is an antibody fragment. This is clearly within the scope of Applicants' election.

Claim 15 is withdrawn.

III. Rejections under 35 U.S.C. §102

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Ladner *et al.* (U.S. Patent No. 5,223,409).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30, and 35 were rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Griffiths *et al.* (U.S. Patent No. 5,962,255).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. § 102(e) as allegedly anticipated by Wang *et al.* (U.S. Patent No. 6,833,441).

Applicants respectfully traverse these rejections.

A. The Present Claims

The present claims relate to an expression vector for expressing a multimeric polypeptide anchored on a surface of a genetically replicable package formed by a host. The expression vector comprises a vector segment encoding a polypeptide sequence having (i) a first polypeptide segment, (ii) a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent, and (iii) a third polypeptide segment having therein an anchoring peptide sequence for anchoring the multimeric polypeptide to said surface of the genetically replicable package. The second polypeptide segment is between the first polypeptide segment and the third segment. The cleavable peptide sequence is cleaved by the proteolytic agent, whereby the first segment associates with the third segment to form the multimeric polypeptide.

B. The Cited References

LADNER ET AL. relate to a method of obtaining a nucleic acid encoding a binding protein. In this method, a gene obtained by random mutagenesis of a limited number of codons is fused to a genetic element which causes the resulting chimeric expression product to be displayed on the outer surface of a genetic package (abstract). Genetic variation is achieved through variegation of DNA yielding a mixture of DNA molecules encoding different but related potential binding proteins (see column 7, lines 50-54). The hybrid genes comprise a first DNA sequence which encodes a potential binding domain for the target of interest and second DNA sequence which encodes an outer surface protein to display the protein on the outer surface of the package.

GRIFFITHS ET AL. describe a recombinant vector that encodes a first and a second polypeptide component of members of a specific binding pair using recombination between first and second vectors comprising the nucleic acids encoding the sbp members to produce a recombinant vector encoding a first and a second polypeptide chain component of a sbp member.

WANG ET AL. provide techniques for specific assembly of monomeric polypeptides to form a heterodimer.

C. Analysis

According to the M.P.E.P. § 2131, "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference".

1. Rejection over Ladner *et al.*

Ladner *et al.* teach a chimeric protein for display on the outer surface of a genetic package such as a phage. Nowhere do Ladner *et al.* teach having a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent such that upon protease cleavage, the first segment and third segment associate to form the multimeric peptide. Examiner kindly notes that Ladner *et al.* disclose use of a protease cleavage sequence between two peptide sequences, the ipbd gene and the Pf3 coat-protein gene (column 57, lines 39-45). However, Ladner *et al.* do not disclose subsequent association of the ipbd gene fragment and the Pf3 coat protein gene upon protease cleavage. Applicants' element of subsequent association of the two peptide sequences produced upon protease cleavage to form the multimeric peptide is not present in this reference. Therefore, Ladner *et al.* do not disclose each and every element of Applicants' claims.

2. Rejection over Griffiths *et al.*

Griffiths *et al.* fail to teach a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent as in present claim 1. The Examiner states that Griffiths *et al.* disclose a Cre recombinase and refers to it as an enzymatic proteolytic agent of present claims 11, 13, and 30 in a parenthetical (see page 7, lines 11-14 of the Office action mailed August 1, 2006). Applicants respectfully submit that the Cre recombinase that cleaves the loxP site is not a protease but instead is a DNA-cleaving protein, since the loxP site is comprised of DNA, not amino acids. Instead, Griffiths *et al.* teach recombination of first and second vectors to produce a vector encoding both a first and a second polypeptide chain of a sbp member, without making mention of a second polypeptide segment having a cleavable peptide sequence therein. Since the Cre recombinase is not a protease, Griffiths *et al.* do not teach each and every element of Applicants' claims.

3. Rejection over Wang *et al.*

Wang *et al.* fail to teach a second polypeptide segment having therein a cleavable peptide sequence cleavable by a proteolytic agent as in present claim 1. The Wang *et al*. reference is directed to the use of Abus, or antigen-binding units, that are comprised of two peptides with heterodimerization sequences, as described at column 4, lines 6-10. The Examiner refers to a protease site in Wang *et al*. (column 37, lines 1-7) that is present between the heterodimerization sequence (of an Abu) and the coat protein sequence as the cleavable peptide sequence cleavable by a proteolytic agent in the second polypeptide segment of the present claims. However, cleavage with the protease in Wang *et al*. is not designed to cause association of the first sequence (heterodimerization sequence) with the second sequence (coat protein sequence), but is instead designed to release the Abus from the phage particles (see column 37, lines 7-10)

Furthermore, as described at column 40, lines 12-13, the vector expresses two proteins rather than a single polypeptide sequence having three polypeptide

segments as in the present claims. Wang *et al.* make no mention of a second polypeptide segment having a cleavable peptide sequence therein.

Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 102.

IV Rejections under 35 U.S.C. §103

Claims 1-4, 6, 11, 13, 16-21, 25-26, 30-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Ladner *et al.* and Goers *et al.* (U.S. Patent No. 4,867,973).

Claims 1-4, 6, 11, 13, 16-21, 25-26, 29-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Griffiths *et al.* and Goers *et al.*

Claims 1-4, 6, 11, 13, 16-21, 25-26, 29-31, and 35 were rejected under 35 U.S.C. §103 as allegedly obvious over Wang *et al.* and Goers *et al.*

These rejections are respectfully traversed.

A. The Present Claims are described above.

B. The Cited References

LADNER ET AL. is described above.

GOERS ET AL. relate to antibody-therapeutic agent conjugates having a therapeutic agent covalently attached to an antibody or antibody fragment.

GRIFFITHS ET AL. is described above.

WANG ET AL. is described above.

C. Analysis

According to the M.P.E.P. § 2143, "to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of

success. Third, the prior art references (or references when combined) must teach or suggest all the claim limitations."

1. Rejection over Ladner *et al.* in view of Goers *et al.*

The deficiencies of Ladner *et al.* are discussed above. One of skill in the art would not modify the teaching of Ladner *et al.* to use a second protease cleavage site between a gene of interest and a viral coat protein because the Ladner et al. reference provides no teachings that upon protease cleavage, the gene of interest would assemble with the viral coat protein. Rather, the expected result would be two proteins that cannot assemble.

With regard to claims 2-7, while Ladner *et al.* teach the display system may be utilized to develop antibodies (column 15, lines 65-68), further reading reveals "its primary utility resides in the development of binding proteins which are not antibodies or even variable domains of antibodies" (column 15, line 68 through column 16, line 2). Thus, Ladner *et al.* is not particularly concerned with the difficulties of developing anchored antibodies.

Nor does Goers *et al*. provide the missing teaching as this reference makes no mention of an expression vector for expressing a multimeric polypeptide as presently claimed. Instead, Goers *et al.* is cited merely for a teaching of a urokinase peptide cleavage sequence.

2. Rejection over Griffiths *et al.* in view of Goers *et al.*

The deficiencies of Griffiths *et al.* are discussed above. Nor would one of skill in the art modify Griffiths *et al.* to include a second polypeptide segment having a cleavable peptide sequence as the added sequence would affect folding of the sbp members. Nor is there any guidance for including a second polypeptide segment and addressing the problems associated therewith, which include efficiency of the cleavage and/or purification from the cleavage enzyme.

Nor does the teaching in Goers et al provide the missing teaching. In fact, Goers *et al.* make no mention of an expression vector. Instead, Goers *et al.* is cited merely for teaching a urokinase peptide cleavage sequence.

3. Rejection over Wang *et al.* in view of Goers *et al.*

The deficiencies of Wang *et al.* are discussed above. Nor would one of skill in the art modify Wang *et al.* to include a second polypeptide segment having a cleavable peptide sequence as the proteins are separately produced. Goers *et al.* also fail to make up for this deficiency as the reference makes no mention of an expression vector as presently claimed.

As the references, alone or in combination, fail to teach or suggest all the claim limitations, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. § 103.

If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4410.

Respectfully submitted

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